

allegedly anticipated by each of Hamilton *et al.*, *Science* **1999**, 286, 950-952 (hereinafter "Hamilton article"), by the inventor's presentation at the EMBO workshop in Leysin, Switzerland, on February 25-28, 1999 (IDS C6) (hereinafter "Leysin presentation"), and the poster presentation by Hamilton *et al.* at the 9th International Congress on Molecular Plant Microbe Interactions on July 25-30, 1999 (IDS C7) (hereinafter "Hamilton poster").

Claims 1, 5 through 17, 21, 26 through 29, and 32 through 34 also stand rejected under 35 U.S.C. §103 as allegedly obvious over Waterhouse *et al.*, *Proc. Nat. Acad. Sci.*, 1998, 95, 13959-64 (hereinafter "Waterhouse") and Wassenegger, *Plant Mol. Biol.* 1998, 349-362 (hereinafter "Wassenegger") taken with Dougherty, *Curr. Opin. Cell Biol.*, 1995, 7, 399-405 (hereinafter "Dougherty").

The above listed objections and rejections constitute the entirety of the grounds set forth in the Official Action dated June 21, 2001, for refusing allowance of this application. Each of the rejections and objections is respectfully traversed for the reasons set forth below.

THE PRESENT CLAIMS FULLY SATISFY THE REQUIREMENTS
OF 35 U.S.C. §112, SECOND PARAGRAPH

As a preliminary matter, Applicants are perplexed by the contention in the Official Action at page 3 that the claims do not read on the elected species, *i.e.*, a plant. Claim 1, as most recently amended, reads in pertinent part "A method of determining the occurrence of target gene silencing **in a plant...**" [*Emphasis supplied.*] Claims 5 through 11, 21, and 32 through 34 all depend, directly or indirectly, from claim 1. By statute (35 U.S.C. §112, paragraph 4), all the limitations of a claim are incorporated by reference into its dependent claims. Accordingly, Applicants respectfully

maintain that claims 1, 5 through 11, 21, and 32 through 34 do in fact read on the elected species.

Applicants respectfully take issue with the Examiner's contention that claim 1 is indefinite for not reciting a specific process for analyzing nucleic acid extracts for the presence of SRMs. According to M.P.E.P. § 2173.02,

[d]efiniteness of claim language must be analyzed, not in a vacuum, but in light of:

- (A) The content of the particular application disclosure;
- (B) The teachings of the prior art; and
- (C) The claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made.

Applicants respectfully assert that while Northern blot analysis is exemplified in the specification, the claims need not be limited to those methods. Indeed, it is well-settled that "....a patent need not teach, and preferably omits, that which is well known by those of skill in the art." Hybritech v. Monoclonal Antibodies, Inc., 231 U.S.P.Q. 81 (Fed. Cir. 1986). Those skilled in the art are capable of detecting the presence of SRMs by a variety of methods, including, without limitation, RNAase protection, immunofluorescence with RNA sequence specific antibodies, isolation of RNA, followed by reverse transcription and sequencing of the resulting cDNA, and nuclear and/or cytoplasmic run-on assays. In summary, it cannot reasonably be maintained that claim 1 is indefinite for failing to recite one specific method of analyzing a nucleic acid extract.

The relevant inquiry in determining whether a given claim satisfies the requirements of 35 U.S.C. §112, second paragraph, is whether the claim sets out and circumscribes a particular area with a reasonable degree of precision and particularity such that the metes and bounds of the claimed invention are reasonably clear. In re Moore, 169 U.S.P.Q. 236 (CCPA 1971). Applicants also respectfully disagree that the

lack of apparent correlation between the presence of SRMs and any other phenotype renders claim 1, and, by extension, its dependent claims, unclear. In the present case, the specification does indeed teach that the presence of SRMs in and of itself is correlated with the occurrence of gene silencing in a wide variety of contexts, e.g., co-suppression, transgene silencing, systemically induced silencing, viral defense, etc. (see Example 1). The phenomenon is also observed in both plants and animals (see Example 2). This is certainly unexpected in view of the prior art but it is not unclear in the light of the specification.

In light of all the foregoing, Applicants respectfully submit that the metes and bounds of the present claims would be readily apparent to one of ordinary skill in the art. Accordingly, Applicants request that rejection of claims 1, 5-11, 21, 32 and 34 under 35 U.S.C §112, second paragraph, be withdrawn upon reconsideration.

THE PRESENT CLAIMS FULLY SATISFY THE REQUIREMENTS
OF 35 U.S.C. § 102(a)

According to 35 USC § 102(a),

A person shall be entitled to a patent unless - (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, **before the invention thereof by the applicant for patent.**

[*Emphasis supplied.*] The three references cited as allegedly anticipatory have all been published by one or both of the Applicants.

The priority date of the present application is October 27, 1999. The Hamilton Science article was published by both Applicants on October 29, 1999. Thus, the publication of this article by definition does not antedate the invention of the subject matter of the present application. Accordingly, the

rejection of claims 1, 5-10, 12-17, 21, 26-29 and 32-34 based on Hamilton et al. is improper and should be withdrawn.

Claims 1, 5-10, 12-17, 21, 26-29 and 32-34 stand rejected under 35 U.S.C. 102(a) as allegedly anticipated by a meeting presentation at Leysin, Switzerland. These overheads (IDS-C6) were presented by one of the Applicants in Switzerland less than a year before applicants earliest effective priority date. Claims 1, 5-10, 12-17, 21, 26-29 and 32-34 also stand rejected under 35 U.S.C. §102(a) as allegedly anticipated by Hamilton and Baulcombe. (poster presentation July 25-30 1999, IDS-C7). Neither of these references satisfy the condition of §102(a) that publication occurred "before the invention thereof by the applicant for patent". It should be logically self-evident that the publication relating to use of methods for isolation of SRMS could not have occurred before the invention thereof by Baulcombe et al. The same is true of the Hamilton and Baulcombe poster (C7) with respect to the relative dates of publication and discovery of PTGS in tobacco.

In light of the foregoing, Applicants respectfully submit that each of the above-noted rejections under 35 U.S.C. §102(a) is inappropriate in the present case and should be withdrawn upon reconsideration.

THE PRESENT CLAIMS FULLY SATISFY THE REQUIREMENTS
OF 35 U.S.C. § 103

The Examiner has rejected claims 1, 5-10, 12-17, 21, 26-29 and 32-34 under 35 U.S.C. §103(a) as allegedly unpatentable over Waterhouse et al. and Wassenegger et al. taken with Dougherty et al. In connection with this rejection, the Examiner asserts that "...in view of the teachings of Dougherty et al. it would have been prima facie obvious for one of ordinary skill in the artto modify the collective teachings of Waterhouse et al. and Wassenegger et al. by identifying small RNA molecules that are approximately 10-75

nucleotides in length by Northern analysis with a reasonable expectation of success." Applicants respectfully submit that the Examiner has failed to present a *prima facie* case of obviousness based on the cited references.

According to MPEP § 2142,

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

At the outset, the proposition that Applicants could reasonably expect success is absolutely contradicted by the dates of the cited publications. Dougherty was published in 1995, which is 3 years before Waterhouse and Wassenegger. Moreover, those authors were clearly aware of Dougherty because it is cross-referenced in both Wassenegger [17 therein] and Waterhouse [19 therein].

Waterhouse stated (page 13962) "...there have been a number of models proposed for the induction and operation of PTGS involved with antisense, co-suppression and virus resistance (4, 5, 19 [Dougherty], 20), but none completely fits the observed results...". [Emphasis supplied.]

Wassenegger refers (page 356) to [17] [Dougherty] in the context of a proposed length of RNA molecule, but then immediately counsels that there is no evidence for this (as discussed at length in the previous Response).

Evidence that the claimed invention is not *prima facie* obvious, (because there was no reasonable expectation of success), is found in the historical fact that Wassenegger et al. and Waterhouse et al., while being aware of Dougherty, and the appreciation that methods for post-translational gene silencing were an art-recognized goal, did not in fact arrive at the invention. Instead, based on their own novel and unexpected results, Applicants did.

Furthermore, the rejection under §103 should be withdrawn upon reconsideration because the claimed invention fulfills a long-felt need that others had failed to fill. MPEP § 716.04. Applicants' findings were taken up and subsequently published in the highly prestigious journal *Science*, which is certainly not one which publishes mere confirmations of the prior art. This historical fact simply bears out the comments made in our previous Response, *i.e.*, that there was huge uncertainty in the art at the date of the present invention and success was not achieved until Applicants reduced the invention to practice.

Moreover, Applicants respectfully submit that it is only with the benefit of hindsight that the present invention could be said to be obvious. It has long been agreed that hindsight is impermissible in obviousness determinations. See, *e.g.*, *In re Rouffet*, 47 USPQ 2d 1453, 1457-8 (Fed. Cir., 1998).


In summary, evidence has been presented that there was no reasonable expectation that Applicants would succeed in reducing the present invention to practice; thus the Examiner has not made out a *prima facie* case of obviousness. Further, evidence of favorable secondary considerations already made of record has been reiterated. Based on the foregoing arguments, Applicants respectfully request that the rejection of claims 1, 5, -17, 21, 26-29, and 32-34 under 35 U.S.C. § 103 be withdrawn upon reconsideration.

CONCLUSION

Applicants believe that the present communication is completely responsive to the Office Action of June 21, 2001. In view of the foregoing remarks, it is respectfully submitted that all rejections have been overcome. Accordingly, it is respectfully urged this application be passed expeditiously to issue.

In the event the Examiner is not persuaded as to the allowability of any claim, and it appears that any outstanding issues may be resolved through a telephone interview, the Examiner is requested to telephone the undersigned attorney at the phone number given below.

Respectfully submitted,
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